REMARKS

1. Election/Restriction Requirements

It is noted that the Examiner has maintained the restriction requirement, so that prosecution will now proceed on the claims of Group II, namely claims 69-94, 100 and 133-141.

2. Information Disclosure Statement

The Examiner has indicated that the Information Disclosure Statement (IDS) filed on February 15, 2002 has only been partially considered, apparently due to some non-legible entries on the PTO 1449 Form submitted with the IDS. It is not apparent to the undersigned why these entries were non legible, because the copies in Applicant's file are clear, dark and fully legible. In any event, enclosed herewith are fresh copies of the 1449 Forms initially submitted with Applicant's IDS of February 15, 2002. Although the 1449 Forms may have not been legible as contained in the Examiner's files, the references per se were apparently legible, and since the references were submitted before the mailing date of a first action on the merits, Applicants submit that the references should be considered without the payment of any fee under 37 CFR 1.97 or 1.17(p). If, however, the Examiner determines that either a certification under Rule 1.97 or the payment of a fee is required for consideration of all of the references, then the Examiner is authorized to charge the required fee under 37 CFR 1.17 and 37 CFR 1.97 to Deposit Account No. 02-2448, which deposit account is also referenced at the end of this response.

3. Specification

The Examiner has objected to several terms in the specification as being trademarks which are not properly indicated in the application. Applicants have amended the trademark CARBOPOL® as suggested by the Examiner. However, the other terms noted by the Examiner, Invitrogen, Sigma and Dako, have not been so amended because those terms are company names, and not strictly speaking trademarks.

4. Rejections Under 35 USC 112, First Paragraph, Relating to Written Description

Claims 69-94, 100 and 133-141 have been rejected under section 112, first paragraph, for alleged lack of written description for several reasons enumerated on pages 4-8 of the Office Action. Each of those points is addressed below.

4.1 Objection of Claims 69-94, 100 and 133-141

The Examiner has objected to the phrase in the claims which recites use of an "IL-5 analogue wherein at least one foreign T_H epitope is introduced into the amino acid", specifically objecting to the terms "analogue" and "foreign T_H eptitope".

A. Analogue

Applicants submit that this term is indeed fully described and supported by the specification in combination of both structure and function. As defined by amended claim 133, the term "IL-5 analogue" must possess three characteristics; namely (1) it must include a substantial fraction of IL-5 B-cell epitopes, meaning that the analogue must cross-react to a significant degree with wild-type IL-5 (see the specification in the paragraph bridging pages 24-25); (2) it must include at least one foreign T_H epitopes, and (3) it must be capable of inducing antibodies that cross-react with unmodified IL-5, that is the animal's autologous IL-5 polypeptide. Thus, The IL-5 analogue is structurally defined by a combination of the amino acid sequence of the animal's autologous IL-5 polypeptide into which has been inserted at least one foreign T_H epitope. The IL-5 analogue is also functionally defined as capable of inducing antibodies that cross-react with unmodified IL-5. This is in full compliance with both 35 USC 112, first paragraph and the USPTO's written description guidelines.

B. Foreign T_H Epitope

The term "T_H epitope" refers to a class of products which are well understood by those skilled in the art, and have a well known function, namely the ability of the amino acid sequence constituting the epitope to bind to an MHC class II molecule and be presented to the surface of an APC and to stimulate T-cells. See for example a description at page 19, line 31 – through page 20, line 17. Various T_H epitopes are known in the art and are enumerated in the specification at, for example, page 29, line 24 through page 31, line 5. While there are many T_H

epotipes known, and others may be discovered in the future, It is simply not true, as characterized by the Examiner, that the "foreign T_H epitopes" of the present claims have "no required structure and/or function". Such epitopes have well understood structural and functional characteristics (as noted above), and such characteristics are well understood by those skilled in the art. The Examiner seems to fail to recognize that a person skilled in the relevant art, which is a skilled immunologist, reads the present application and claims with a high level of knowledge, and is well able to understand and comprehend the scope of the term "foreign T_H epitope." Understanding such a term by a skilled immunologist is simply no different than a skilled mechanical engineer understanding that the term "elastic member" can encompass both a mettle spring and a rubber band. Applicants submit that a proper understanding of the skilled artisan and the art relevant to the present application easily leads to a conclusion that the term "foreign T_H epitope" would be fully understood, and is therefore in compliance with 35 USC 112, first paragraph.

4.2 Claims 69-91, 100 and 134-141

The objection to these claims with respect to the phrase "subsequence" has been rendered moot by the cancellation or amendment of the relevant claims.

4.3 Claims 70-84 and 134-141

While these claims have been cancelled and/or amended to obviate some of the objections, there still remains the Examiner's objection to the terms "substitution and/or deletion and/or insertion and/or addition". Nevertheless, claim 133 as amended further defines the modifications as being limited to those that still preserve "a substantial fraction of IL-5 B-cell epitopes". As noted above, this aspect is discussed in the specification in the paragraph bridging pages 24-25. Applicants submit that this amendment obviates the Examiner's objection.

4.4 Claims 71-75 and 134-141

Applicants submit that these objections, referred to in the Office Action in the paragraph bridging pages 6 and 7, have been rendered moot in view of cancellation and/or amendments to the claims.

4.5 Claims 69-94, 100 and 134 - 141

The Examiner has objected to the terms "foreign T-cell epitope is promiscuous" and/or "natural promiscuous T-cell epitope". This objection seems to be somewhat repetitive of the objection discussed above, but as discussed above, these terms are of a type which are well understood by those skilled in the art, such as a skilled immunologist, and are moreover well described in the specification, for example, pages 29-31. Applicant's specification describes both the structure and function of the T-helper epitopes and describes numerous known examples common to those skilled in the art.

4.6 Claims 69 and 85

Claim 69 has been cancelled. Claim 85 has been amended to further define that the modifications are with respect to introduction of a foreign T_H epitope. As discussed above, Applicant's specification does indeed provide description of both structure and function in full compliance with 35 USC 112, first paragraph.

4.7 Claims 70-71, 81 and 135 and claims 71 and 84

These claims have been canceled, thereby rendering the objections moot.

In view of the above, Applicants submit that the claims, as amended, are indeed fully supported by the specification and are in full compliance with 35 USC 112, first paragraph. Therefore, the rejection should be withdrawn.

5. Rejection of Claims 69-94, 100, 133-141 Under 35 USC 112, First Paragraph with Respect to Enablement

These claims have been rejected for allegedly enablement with regard to several aspects enumerated on pages 8-15 of the Office Action.

5.1 Claims 69-94, 100 and 133-141 with Regard to the Term "Immunogenically Effective Amount"

The Examiner objects to this term on the basis that it could be interpreted to "illicit a general immune response". The Examiner, however, seems to fail to recognize further definition

in the claims which states that "immunization of the animal with the IL-5 analogue uses antibodies against the animals autologous Il-5 polypeptide." This indeed recites a specific immune response, as further described in the specification at, for example, page 19, the first full paragraph. Applicants submit that the Examiner's rejection, therefore, is not well founded.

5.2 Claims 69-94, 100 and 133-141

The Examiner here objects to the scope of the terms "analogue" and "foreign T_H eptitope", referencing, among other things, the unpredictability of the art.

First of all, this rejection seems to be rather duplicative of the Examiner's rejection for alleged lack of written description, which rejection has been sufficiently discussed and rebutted in the remarks set forth above.

The Examiner's objection also fundamentally fails to appreciate the difference between the function of the claims as compared to the specification. The Examiner's rejection only focuses on the claim terminology without giving proper appreciation to the vast and relevant teachings in Applicant's specification. The specification provides a large amount of teachings with regard to preparation of suitable IL-5 analogues useful in the present invention. The only functionality of the IL-5 polypeptide which needs to be preserved in the present application is the presence of at least a substantial fraction of IL-5 B-cell epitopes as specifically recited in amended claim 133. The specification provides extensive teachings about how to prepare such IL-5 analogues, and it must be expected that one skilled in the art seeking to practice the present invention would follow those teachings and would not work in a manner that is contrary to the teachings of the present application. Thus, Applicant's specification properly teaches one skilled in the art how to practice the claimed invention because "it is the function of the specification, not the claims, to set forth the 'practical limits of operation' of an invention". *In re Johnson*, 194 USPQ 197, 195 (CCPA 1977). While it might arguendo be true that someone could introduce foreign material into the IL-5 polypeptide in a manner that could completely destroy the immunogenic properties, such person would then not be following the teachings of the present application, and this surely is not the proper view of enablement under 35 USC 112.

5.3 Claims 69-94, 100 and 134-141

The Examiner here has objected to the term "subsequence". This rejection has been rendered moot by cancellation and/or amendment of the claims.

5.4 Claims 69 and 85

Claim 69 has been cancelled and claim 85 has been amended, thereby obviating this objection.

5.5 Claims 69 and 100

Claim 69 has been cancelled. Claim 100 has been amended to obviate the Examiner's apparent objection to the terms "preventing" and "ameliorating".

5.6 Claims 71-75 and 134-141

The Examiner has also objected to the claims with regard to various terminology as set forth on pages 14-15 of the Office Action. These objections have been rendered moot by either cancellation or amendment to the claims.

In view of the above, Applicants submit that the rejections under 35 USC 112, first paragraph, for alleged lack of enablement should be withdrawn.

6. Rejections Under 35 USC 112, Second Paragraph

The Examiner has first objected to the phrase "substantial fraction". However, this term is well defined in the paragraph bridging pages 24 and 25 of the specification in a manner that would be well understood by those skilled in the art.

Claims 69-72 and 84 have been cancelled, thereby rendering that objection moot.

Claim 74 has been included by the Examiner in the objections, but it is not seen that any particular term in claim 74 has been indicated as being objectionable. It appears, therefore, the Examiner was mistaken in including claim 74 in the rejection set forth on page 16.

In view of the above, reconsideration and withdrawal of the rejections under 35 USC 112, second paragraph are requested.

7. **Rejections Under 35 USC 103**

Claims 69-94, 100 and 133-141 have been rejected under 35 USC 103 for obviousness over a combination of Balun et al. in view of Steinaa et al. and Foster et al., or over Dalum et al. in view of Mouritsen et al. and Foster et al.

First of all, any rejections based on Steinaa et al. are improper because that reference is not properly prior art to the present application. Steinaa et al. is a published US application which bases priority back to a provisional application filed on October 20, 1998, ostensibly an effective filing date under 35 USC 102(e) as suggested by the Examiner. However, Steinaa et al. is assigned to M&E Biotech A/S, which later changed its name to Pharmexa A/S, which is the assignee of the present application. Since Steinaa et al. and the present application are owned by the same entity, Steinaa et al. is excluded as prior art based on its US filing date by virtue of the exception provided in 35 USC 103(c).

Therefore, the only prior art rejection relevant to this case is that based upon a combination of Dalum et al. in view of Mouritsen et al. and Foster et al.

The Examiner urges that Mouritsen et al. discloses a method of vaccination of self proteins, by recombinantly introducing foreign T_H epitopes into said self proteins, and additionally discloses tetanus toxoid has a T_H lymphocyte stimulating epitope. While it is true that technology existed in 1999 for inducing active immunity against self-proteins, the proper question for purposes of obviousness of the present invention is whether one skilled in the art would expect that it would be possible to target IL-5, the subject of the present claims.

To the best of Applicant's knowledge, it has never before been demonstrated that it is possible to vaccinate actively against IL5 and obtain a down-regulation of the activity thereof. And, absent any citations of prior art that substantiate that it would be possible to actively vaccinate against IL5 and obtain a down-regulation of this molecule and its pathology-related effects, Applicant submits that a broad patent protection is justified for the application of this novel approach. One skilled in the art at the time of Applicant's invention would not have a reasonable expectation of success, the standard for obviousness under 35 USC 103.

One important reason for the prior art falling to suggest or demonstrate active vaccination against IL5 is most likely the fact that murine IL5 is known to be a B-cell differentiating factor, hence the IL5

alias "BCDF" (B-cell differentiating factor). Thus, in mice, IL5 is responsible for induction of proliferation of pre-activated B-lymphocytes and their differentiation.

Applicants submit that the fact that IL5 in mice induces B-cells to proliferate and differentiate teaches against active vaccination against this molecule, since active vaccination inherently requires that B-cells proliferate and differentiate. In other words, the skilled person would expect that the presence of IL5 is important or even necessary in order to raise antibodies against any antigen and that down-regulation of IL5 via active immunization would be a self-contradictory strategy - the antibodies induced would inhibit their own production.

Nevertheless, Applicant has demonstrated that vaccination against IL5 in mice does indeed lead to induction of anti-IL5 antibody production, and: that the activity of IL5 is reduced, as demonstrated by reduction in eosinophil counts (reported in the specification). Furthermore, and this is equally important, no adverse effects have been observed in the vaccinated animals.

So, absent any teaching, suggestion or indication in the prior art that it is feasible to immunize against autologous IL5, the presently claimed approach cannot be obvious over the Examiner's cited combination of references.

In view of the above, Applicants submit that the present claims are indeed obvious over the Examiner's attempted combination of prior art references, so that the claims indeed define a patentable invention with the meaning of 35 USC 103.

8. Double Patenting Rejection

The claims have been rejected for obviousness-type double patenting over claims 1-29 of U.S. Patent 6,746,669. This objection could be overcome by the filing of a terminal disclaimer, but Applicants elect to defer directly addressing this objection until such time as the language of allowable claims in the present application is determined.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned below at 714-708-

8555 in Costa Mesa, CA to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), the Applicant respectfully petitions for a three (3) month extension of time for filing a response in connection with the present application and the required fee of $1020.00 should be charged to Deposit Account No. 02-2448.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By: _____

Leonard R. Svensson
Registration No. 30, 330

P.O. Box 747
Falls Church, VA 22040-0747
(714) 708-8555

LRS/lmt
Attachments

Certificate of Transmission
I hereby Certify that this correspondence is being facsimile transmitted to the Patent and Trademark Office:
On June 15, 2005
Date
Signature
Typed or printed name of person signing certificate